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Customer No. 054042

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:				
	Felicia Grases Freixedas	:	Confirmation No.:	5118
Serial No.:	10/595,709	:	Art Unit:	1614
Filing Date:	May 5, 2006	:	Examiner:	Charlesworth Rae
For:	Myoinositol Hexaphosphate for Topical Use			

April 1, 2009

MAIL STOP: Amendment
Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO JANUARY 6, 2009 OFFICE ACTION

Claims 8-19 are pending and under examination in the above-referenced application. Applicant has not amended or canceled any claims in response to the January 6, 2009 Office Action.

In the January 6, 2009 Office Action, the Examiner indicated that claims 8-19 are rejected under 35 U.S.C. 103(a) as obvious over Kamiya et al., in view of Bisset et al. as evidenced by Horrobin et al.. Specifically, the Examiner indicates that Kamiya et al. disclose methods of treating or preventing aging-associated disease caused by a decrease in the expression of Klotho protein in animals or humans by using a composition comprising phosphorous containing compounds by any desirable route. Since Kamiya et al. does not specifically teach the method step of topical application of myo-inositol hexaphosphate, the Examiner relies on Bisset et al. as disclosing methods of treatment for improving the visual appearance of skin comprising administering topical compositions comprising myoinositol compounds. Additionally, the Examiner relies on Horrobin et al. to show that ectopic calcifications involve various soft tissues, including blood vessels, kidney, skin and brain.

In response, applicant respectfully traverses the Examiner's ground of rejection. Applicant disagrees with the Examiner's interpretations of the disclosures of the cited references and maintains that the combination of these references does not teach or suggest each and every element of applicant's claimed method.

Specifically, Kamiya et al. provide a laundry list of possible diseases to be prevented or treated under the heading "disease caused by a decrease in the expression of Klotho protein". This is a broad genus of diseases which one skilled in the art would recognize as being very expansive. Each particular disease caused by a decrease in the expression of Klotho protein has its own specific characteristics and etiology. Drawing clinical conclusions by way of extrapolation from laboratory data is highly unpredictable and unreliable especially when trying to generalize for many diseases under a particular problem. As it will subsequently be proven, this extrapolation for ectopic calcification is not true at all.

According to the abstract and paragraphs 40 and 43 of Kamiya et al., ornithine is the agent responsible for the therapeutic effect over diseases caused by a decrease in the expression level of Klotho. See paragraphs 40 and 43 respectively below:

> "Also provided are a therapeutic or preventing agent for premature aging-like syndrome of homozygous Klotho mutant animals and a feed for the treatment or prevention of the syndrome, which comprise ornithine or a salt thereof as an active ingredient" (abstract) and *"The therapeutic or preventing agent for diseases caused by a decrease in the expression level of Klotho protein in animals or humans of the present invention comprises ornithine or a salt thereof, and if necessary, may comprise one or more pharmaceutically acceptable carriers..."* (Emphasis added)

and

> "The therapeutic or preventing agent for disease caused by a decrease in the expression level of Klotho protein of the present invention is produced according to an arbitrary method well known in the technical field of pharmaceutics by mixing ornithine or a salt thereof with a carrier, as may be required."

Additionally, the disclosure of compounds containing phosphorous at paragraph 78 of Kamyla et al. indicates that the purpose of these divalent cationic metal and/or phosphorus compound is to facilitate the administration in the feed or food and drink. See paragraph 78 below:

> "The feed or food and drink of the present invention preferably comprises at least one compound selected from the group consisting of compounds containing a divalent

cationic metal and compounds containing phosphorus."

Applicant maintains that there is no disclosure of the biological effect of these compounds together with ornithine. These compounds are disclosed when referring to feed or food and drink, never when considering the therapeutic effect of the agent (ornithine) capable of preventing or treating diseases caused by a decrease in the expression level of Klotho protein. Furthermore, paragraph 78 indicates that only one compound containing a divalent cationic metal may be used, thereby eliminating the essentiality of any compound containing phosphorous. Therefore, compounds containing phosphorous is not deemed essential for Kamiya et al. and consequently a skilled person in the art would never establish a direct relationship, i.e. therapeutic agent to disease, between compounds containing phosphorus, e.g. phytic acid, and the disease, e.g. ectopic calcification.

In addition, applicants maintain that the disclosure of compounds containing phosphorous which can be used for Kamiya et al., phytic acid is mentioned as a by-product of the hydrolyzation of phosphoric esters which produce adenosine triphosphate. Among the list of compounds which may be used is hydroxyapatite, which is incompatible with the object of the present invention since hydroxyapatite is responsible of pathological calcifications and therefore a compound to be removed. Consequently, it would be obvious to a skilled person in the art that phytic acid is not the compound responsible of preventing and/or treating diseases caused by a decrease in the expression level of Klotho protein. (see also paragraph 78 of Kamiya et al.).

In addition, applicants maintain that the use of phytic acid as the compound containing phosphorus or the use of possible phosphoric esters containing it is not disclosed in any working example of Kamiya et al.. Only inorganic salts ($CaHPO_4$ and KH_2PO_4) are disclosed. One skilled in the art would not consider phytic acid as a substitute for these compounds. Furthermore, there is no disclosure of a direct effect on ectopic calcification. Instead, Kamiya et al. indicate at paragraph 107 that "[t]he above results indicated that ornithine was effective in raising the expression level of kidney Klotho protein, raising the blood sugar level, lowering the serum inorganic phosphorus level and increasing the body weight of male homozygous klotho mutant mice, i.e., ornithine had inhibitory effects on premature aging-like syndrome of the mice"

and at paragraph 108 that "[t]he weight-increasing effect of ornithine was thus observed also on female individuals", and at paragraph 111 that "[t]he number of deaths was decreased in the groups fed on the feeds containing ornithine as shown above, indicating that ornithine was effective in prolonging life span." According to these paragraphs, it can be concluded that the agent responsible of the biological effect is ornithine and there is no mention about the effect over ectopic calcification.

Applicants maintain that Bisset et al. does not cure any of these deficincies. Rather, Bisset et al. disclose methods of treatment for improving visual appearance of skin comprising administering topical compositions comprising myoinositol compounds. Bisset et al. only disclose compositions for "improving the visual appearance of skin" and/or "regulating atrophy" and/or "skin lightening" and/or "regulating skin smoothness" as defined in columns 3 and 4. Although it is not mentioned in detail how and where the composition acts biologically, according to the intended cosmetic effects it is obvious that reaching the blood stream is not expected. Indeed, along all the text, the word "cosmetic" is generally used appointing the cosmetic purpose of the formulation and consequently with no intention for a therapeutic systemic effect inside the body. All the objects of Bisset's invention are focused on the outer part of the skin, completely opposite to the instant application, wherein the outer part of the skin is just use as an entrance way in order to eventually reach the blood stream. Applicants point the Examiner's attention to the previous filed communication wherein the different layers of skin and the effects of phytic acid on these layers are discussed in connection with overcoming the rejection over Znaiden et al. In contrast, applicants have demonstrated the absorption of the active compound into the blood vessels and systemic effect, whereas Bisset et al. refers to a superficial application .

In view of the remarks above, applicants maintain that the combination of cited references does not disclose applicants invention and would not lead on skilled in the art to use applicants invention by combining the teaching of these cited references. Accordingly, applicants maintain that claim 8-19 are not rendered obvious by the combined disclosures of Kamiya et al. and Bisset et al. and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Reconsideration and allowance of all the claims herein are respectfully requested.

Respectfully submitted,

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